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4-30-93

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GROUP 180

Applicants: David C. Ward et al.

Serial No.: 07/130,070 Group Art Unit: 1807

Filed: December 8, 1987 Exam'r: Ardin Marschel, Ph.D

For: **MODIFIED NUCLEOTIDES AND METHODS OF PREPARING AND USING SAME**

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3/25/98
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Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

REVOCATION OF POWER OF ATTORNEY OR AUTHORIZATION AND APPOINTMENT OF NEW ATTORNEYS UNDER 37 C.F.R. §1.36

Yale University, a non-profit corporation organized under the laws of the State of Connecticut and having offices at 451 College Street, New Haven, Connecticut 06520, is the assignee of the entire interest in the above-identified patent application by virtue of an assignment recorded with the United States Patent and Trademark Office on February 24, 1982 at Reel 3950, Frames 423-427, in connection with a predecessor application, Serial No. 06/225,223, filed on April 17, 1981. As the assignee, it has reviewed the evidentiary documents and certifies, to the best of its knowledge and belief, that title is in the assignee seeking to take action. Yale University hereby revokes all previous powers and appoints:

Arthur M. Lieberman, Reg. No. 20,042; Keith D. Nowak, Reg. No. 27,367; David A. Kalow, Reg. No. 29,297; Milton Springut, Reg. No. 27,721; John P. Parise, Reg. No. 34,403; John J. Santalone, Reg. No. 32,794; and Ronald C. Fedus, Reg. No. 32,567,

and each of them, all in care of Lieberman & Nowak, 292 Madison Avenue (8th Floor), New York, New York 10017, its attorneys, each with full power of substitution and revocation to prosecute this application, to make alterations and amendments therein, to receive the patent, to transact all business in the Patent and Trademark Office connected therewith and to file any International Applications which are based thereon.

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Signed at New Haven, Connecticut
this 13 day of April 1993 By: Dorothy K. Robinson

Dorothy K. Robinson, Esq.
General Counsel and duly
authorized to sign on
behalf of Yale University

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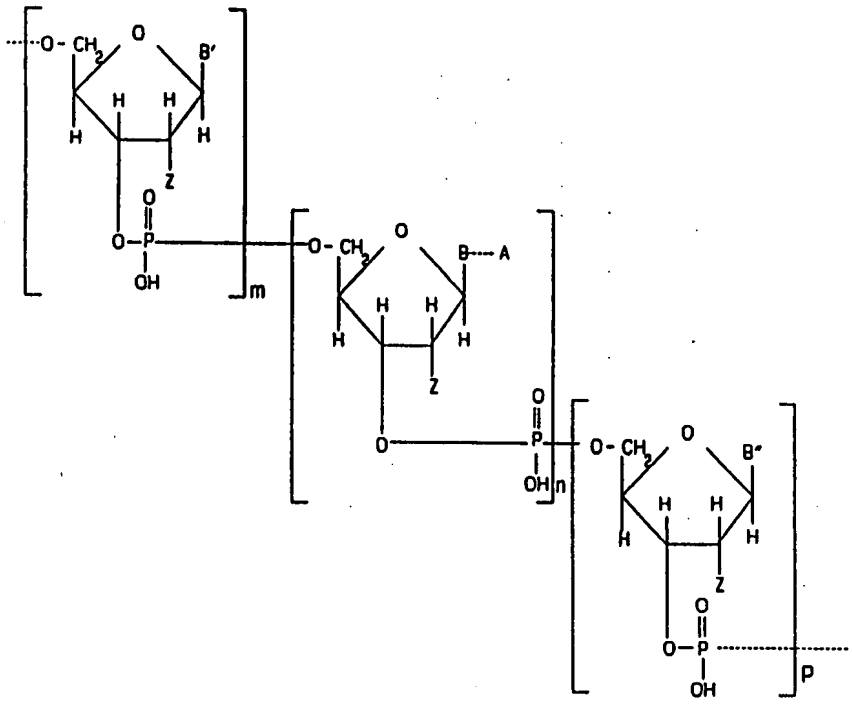
150. A method of detecting the presence or absence of a nucleic acid in a sample which comprises the steps of:

(a) contacting under hybridizable conditions said sample with at least one compound comprising the structure:



wherein each of B' and B" represents a purine, 7-deazapurine, or pyrimidine moiety covalently bonded to the $C^{1'}$-position of the sugar moiety, provided that whenever B' or B" is purine or 7-deazapurine, the sugar moiety is attached at the N^9-position of the purine or 7-deazapurine, and whenever B' or B" is pyrimidine the sugar moiety is attached at the N^1-position of the pyrimidine;

wherein B represents 7-deazapurine or pyrimidine moiety covalently bonded to the $C^{1'}$-position of the sugar moiety, provided that whenever B is 7-deazapurine, the sugar moiety is attached at the N^9-position of the 7-deazapurine, and whenever B is pyrimidine the sugar moiety is attached at the N^1-position of the pyrimidine;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing a detectable signal;

wherein B and A are covalently attached directly or indirectly through a linkage group, said linkage group not interfering substantially with the characteristic ability of said compound to hybridize with said nucleic acid or of A to be detected;

wherein if B is 7-deazapurine, A is attached to the 7-position thereof, and if B is pyrimidine, A is attached to the 5-position thereof;

wherein m, n and p are integers, provided that m and p are not simultaneously 0 and provided further n is never 0; and

wherein z represents H- or HO-; and

(b) detecting said compound or compounds so as to detect said nucleic acid.

126. The method of claim 150 wherein said nucleic acid is derived from a living organism.

127. The method of claim 126 wherein said living organism is selected from the group consisting of prokaryotes and eukaryotes.

128. The method of claim 150 wherein said sample is suspected of containing an etiological agent and said nucleic acid is associated with said etiological agent.

129. The method of claim 128 wherein said sample is of human or animal origin and said etiological agent is selected from the group consisting of bacteria, viruses and fungi.

130. The method of claim 150 wherein said sample comprises a microorganism suspected of containing a nucleic acid which imparts resistance to an antibiotic and wherein said compound comprises a polynucleotide complementary to the nucleic acid of said microorganism which confers resistance to said antibiotic.

134. The method of claim 150 wherein said sample is suspected of containing a nucleic acid associated with a genetic disorder and wherein said compound comprises a polynucleotide complementary to the nucleic acid associated with said genetic disorder.

135. The method of claim 150 wherein said sample is suspected of containing a nucleic acid associated with or absent in thalassemia and wherein said compound comprises a polynucleotide complementary to the nucleic acid which is associated with or absent in thalassemic subjects.

136. The method of claim 150 for chromosomal karyotyping which comprises contacting said sample with a series of said compounds which are complementary to a series of known genetic nucleic acids located on chromosomes.

142. The method of claim 150 wherein said sample is suspected of containing a nucleic acid which codes for expression of a polypeptide associated with a tumor cell and wherein said compound comprises a polynucleotide complementary to the messenger ribonucleic acid transcribed from a deoxyribonucleic acid associated with the production of said polypeptide.

143. The method of claim 142 wherein said polypeptide is α-fetal protein.

152. The method of claim 150 wherein the moiety A is a ligand.

153. The method of claim 152 wherein the ligand is selected from the group consisting of a hapten, an antigen, a cofactor, biotin and iminobiotin.

154. The method of claim 152 wherein the ligand is selected from the group consisting of dinitrophenol, lipoic acid and an olefinic compound.

156. The method of claim 152 wherein the ligand is capable of forming a complex by binding with a detectable polypeptide.

157. The method of claim 156 wherein the detectable polypeptide is selected from the group consisting of an antibody, an enzyme capable of depositing insoluble reaction products, streptavidin and avidin.

159. The method of claim 156 wherein the sample is contacted with the detectable polypeptide after hybridization of the compound or compounds to said nucleic acid under suitable conditions as to form the complex.

160. The method of claim 156 wherein an indicator molecule is associated with or bound to the detectable polypeptide.

161. The method of claim 160 wherein the indicator molecule is fluorescent, electron dense, or an enzyme capable of depositing insoluble reaction products.

162. The method of claim 161 wherein the enzyme is selected form the group consisting of alkaline phosphatase, peroxidase and β-galactosidase.

163. The method of claim 161 wherein the fluorescent indicator molecule is selected from the group consisting of fluorescein and rhodamine.

164. The method of claim 161 wherein the electron dense indicator molecule is selected from the group consisting of ferritin, hemocyanin and colloidal gold.

165. The method of claim 160 wherein the indicator molecule is covalently linked to the detectable polypeptide.

166. The method of claim 160 wherein the detectable polypeptide is indirectly detectable by specifically complexing the detectable polypeptide with a second polypeptide covalently linked to an indicator molecule.

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177. The method of claim 150 wherein said nucleic acid is immobilized on a solid support.

178. The method of claim 150 wherein the moiety A comprises at least 5 carbon atoms.

179. The method of claim 150 wherein the moiety A is non-aromatic.

180. The method of claim 150 wherein B is selected from the group consisting of uracil, cytosine, deazaadenine, deazaguanine.

181. The method of claim 150 wherein the linkage group comprises an olefinic bond at the α-position relative to B.

182. The method of claim 181 wherein the linkage group comprises the moiety $-CH=CH-CH_2-NH-$.

183. The method of claim 181 wherein the linkage group comprises the moiety

$$-CH=CH-CH_2-O-CH_2-\underset{\displaystyle OH}{CH}-CH_2-NH-.$$

185. The method of claim 130 wherein when said microorganism is Streptococcus pyrogenes or Neisseria meningitidis, said antibiotic is penicillin, wherein when said microorganism is Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Streptococcus pyrogenes, or Neisseria gonorrhoeae, said antibiotic is a tetracycline, and wherein when said microorganism is Mycobacterium tuberculosis, said antibiotic is an aminoglycoside.

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